



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-N-2406]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Market Claims in Direct-to-Consumer Prescription Drug Print Ads

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-7285, or emailed to [oir\\_submission@omb.eop.gov](mailto:oir_submission@omb.eop.gov). All comments should be identified with the OMB control number 0910-NEW and title, "Market Claims in Direct-to-Consumer Prescription Drug Print Ads." Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Rd., COLE-14526, Silver Spring, MD 20993-002, [PRAStaff@fda.hhs.gov](mailto:PRAStaff@fda.hhs.gov).

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Market Claims in Direct-to-Consumer Prescription Drug Print Ads--

OMB Control Number 0910-NEW

Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes FDA to conduct research relating to health information. Section 1003(d)(2)(C) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 393(d)(2)(C)) authorizes FDA to conduct research relating to drugs and other FDA regulated products in carrying out the provisions of the FD&C Act.

The marketing literature divides product attributes ("cues") into intrinsic and extrinsic. Intrinsic cues are physical characteristics of the product (e.g., size, shape), whereas extrinsic cues are product-related but not part of the product (e.g., price and brand name) (Refs. 1 and 2). Research has found that both intrinsic and extrinsic cues can influence perceptions of product quality (Ref. 3). Consumers may rely on product cues in the absence of explicit quality information. The objective quality of prescription drugs is not easily obtained from promotional claims in direct-to-consumer (DTC) ads; thus consumers may rely upon extrinsic cues to inform their decisions. Market claims such as "#1 Prescribed" and "New" may act as extrinsic cues about the product's quality, independent of the product's intrinsic characteristics. Prior research has found that market leadership claims can affect consumer beliefs about product efficacy, as well as their beliefs about doctors' judgments about product efficacy (Ref. 4). One limitation of these prior studies is the lack of quantitative information about product efficacy in the information provided to respondents. Research indicates that providing consumers with efficacy information generally improves understanding and facilitates decisionmaking (Refs. 5 and 6).

Efficacy information may moderate the effect of the extrinsic cue by providing insight into characteristics that would otherwise be unknown. Other research has shown that consumers are able to use information about efficacy to inform judgments about the product (Refs. 6 and 7).

The Office of Prescription Drug Promotion (OPDP) plans to investigate, through empirical research, the impact of market claims on prescription drug product perceptions with and without quantitative information about product efficacy. This will be investigated in DTC print advertising for prescription drugs.

### I. Design Overview and Procedure

The design consists of two parts: a main study and a followup study. We will conduct two sequential pretest waves prior to the main study and one pretest prior to the followup study. The purpose of the pretests are to (1) ensure the stimuli are understandable and viewable, (2) identify and address any challenges to embedding the stimuli within the online survey, and (3) ensure the study questions are appropriate and meet the study's goals.

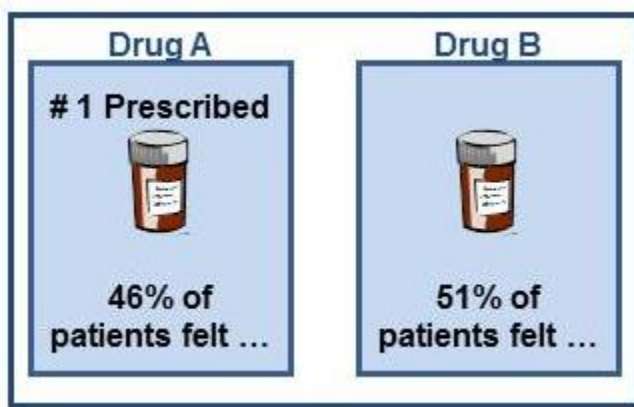
Participants in the main study will be randomly assigned to view one of nine versions of an ad, as depicted in table 1. The two variables of interest are type of market claim (#1 Prescribed, New) and type of efficacy information (High, Low, or None). Efficacy information will be operationalized in the form of realistic quantitative information (for example, "46 percent of patients felt their nerve pain reduced by at least half, compared to baseline").

Table 1.--Main Study Design

	Type of Market Claim		
	#1 Prescribed	New	None (control)
Efficacy Level Information:			
High	A	B	C
Low	D	E	F
None (control)	G	H	I

In the followup study, participants ( $n = 216$ ) will complete a 15-minute paired choice experiment. Participants will be asked to choose between two hypothetical drugs based on print ads, one of which includes a market claim from the Main Study (#1 Prescribed or New). The ads also include different efficacy information (for example, "46 percent of patients felt their nerve pain reduced by at least half, compared to baseline" versus "51 percent of patients felt their nerve pain reduced by at least half, compared to baseline"). Figure 1 depicts an example choice. Participants are asked to indicate which drug they would prefer. They are given 48 such choice sets, which vary in efficacy information and the presence of the market claim.

Figure 1.--Example Choice in the Followup Study



## II. Procedure

Pretests: Each participant will be randomly assigned to view a print ad for a fictitious prescription drug indicated to treat diabetic neuropathy and will be asked to complete an online survey assessing their benefit/risk perceptions, intentions, and attitudes toward the drug. Based on the pretest findings, we will revise and remove poorly performing survey items prior to full-scale testing.

Main study: Each participant will be randomly assigned to view a print ad for a fictitious prescription drug for diabetic neuropathy and will be asked to complete an online survey assessing their benefit/risk perceptions, intentions, and attitudes toward the drug.

Followup study: Each participant will be asked to view a series of pairs of print ads for a product that treats diabetic neuropathy. One ad will contain a market claim. Both ads will contain quantitative efficacy information that varies along a continuum of effectiveness in a series of 48 trials. In each comparison, participants will be asked to choose one of the two drugs.

In the Federal Register of July 20, 2015 (80 FR 42823), FDA published a 60-day notice requesting public comment on the proposed collection of information. Six submissions were received; three from biopharmaceutical companies (AbbVie, Eli Lilly, Merck), two that were anonymous, and one from Danny Weiss, PharmD. The comments from the two anonymous submitters and Dr. Weiss requested the United States ban DTC advertising for pharmaceuticals. This is outside the scope of this project. We summarize and respond to the other comments as follows.

(Comment 1) From AbbVie: Respondents may view "benefits" and "risks" more generally versus "side effects" as a specific inquiry. For example, "side effects" could be interpreted as adverse effects or adverse events, and as such, elicit a much more specific response than "risks" which could be seen more broadly. We suggest that "side effects" be eliminated from question 4 to keep questions 3 and 4 as both general in nature.

(Response) We are interested in recall of both risks and side effects, and so we inquire about both. Inquiring about risks only may artificially reduce the quantity of recall. Moreover, we counterbalance the presentation of questions 3 and 4 in efforts to account for any influence of question ordering. It would be feasible to instead inquire about risks and side effects in separate

questions; however, in our experience, we find that consumers tend to think about risks and side effects together, which makes sense given the typical presentation of risks and side effects in direct-to-consumer promotional materials.

(Comment 2) From AbbVie: The answers to questions 7 through 12 may be biased by attitudes toward advertising in general and may go well beyond the pharmaceutical ad they are shown.

(Response) By asking these questions, we hope to detect any differences in perceived effectiveness and risk between those exposed to different experimental conditions. For example, those exposed to an ad with a #1 Prescribed market claim may perceive the product to be more effective than those in the control condition. We acknowledge participants may bring their own opinions about advertising to the study. However, these opinions tend to be evenly distributed across experimental conditions based on random assignment procedures. Thus, any differences result from the experimental manipulations.

(Comment 3) From AbbVie: We acknowledge we have not seen the test ad; but, we wish to point out that questions 13 and 17 rely on the ad presenting numeric efficacy and safety information that can be interpreted by respondents.

(Response) Prior research has shown that consumers can reach numeric judgments about efficacy and risk despite no numeric information being presented (Ref. 5). As described in our study design (see table 1), we are not manipulating quantitative safety information and not all test ads contain quantitative efficacy information. We have worked with an expert reviewer in OPDP to produce efficacy claims that are realistic for this drug product class.

(Comment 4) From AbbVie: Question 18 relies on the ad presenting information about the seriousness of one or more "side effects" that the respondent could rank. We do not usually

see print ads that present details about the extent of the seriousness of one or more side effects.

In the absence of this presentation, how are respondents to answer this question?

(Response) We find that consumers are generally able to differentiate between the seriousness of various risks and side effects, and also that they can make judgments about the overall (gist) seriousness of the risks and side effects. We ask this question with the intention to detect whether or not exposure to market claims and efficacy information impacts risk perceptions.

(Comment 5) From AbbVie: The answers to questions 21 to 26 may reflect a patient's perception of their doctor rather than the ad. Therefore, the answers may not reflect what was communicated in the ad but rather reflect the patient-doctor relationship (e.g. patient perception of their doctor).

(Response) We are endeavoring to replicate the results of Mitra et al. (Ref. 4), who found that market leadership claims affected consumer beliefs about doctor's judgments.

(Comment 6) From AbbVie: In the table headers for questions 27 and 28, please change "claim" to "statement" so that it matches the text in the question.

(Response) We will make this change.

(Comment 7) From AbbVie: It is beneficial to rotate the order of response choices in questions 27 and 28 as is done in prior questions. Some of the features a-h are broad (b. pictures and images) while some are specific (e. percentages). It would be better to compare the very general features in a question and group the very specific features into another question to compare like features.

(Response) We will make this change.

(Comment 8) From AbbVie: For questions 35 to 38, rather than rank from Strongly Disagree to Strongly Agree, which are absolutes, it would be better to rank by frequency from Never to Always; this moves the response to how often patients perceive this and away from absolutes.

(Response) We acknowledge that it is difficult to rank agree/disagree on all drugs. However, a scale range of Always-Never is unipolar; we can't assess whether respondents think the opposite, e.g., that New drugs tend to be more risky or that the #1 Prescribed drug is more risky. Our intention is to use these items as a moderator when examining the impact of the experimental manipulations (i.e., market claims, efficacy claims) on benefit and risk perceptions, intentions to take the product, and other outcomes. We believe the most relevant scale for this analysis is the current Strongly Disagree to Strongly Agree scale. Although it would be interesting to assess participant responding using both scales, doing so may not add significant value relative to the additional burden it would pose for participants.

(Comment 9) From AbbVie: We suggest that all the features of question 43a to h be stated in the affirmative/positive. For example, question 43h should be worded as "the drug has few side effects" to be consistent with features of question 43a to g that are positively stated.

(Response) The proposed item, "the drug has few side effects," assesses a different outcome than our current question, "the drug has serious side effects." We have also added items assessing "drug cost and/or copay" and "doctor's recommendation." For consistency, we will change the wording so that all features are neutral (for instance: the drug's side effects, opinions of people I know, how often the drug is prescribed).

(Comment 10) From Lilly: Given the proposed FDA research questions, Lilly believes the design is appropriate and the sample size will allow for breakouts by each cell. In advertising



A/B tests, in which this is similar to, all aspects of the stimulus not being tested are held the same in order to reduce bias and isolate the feature being tested. We strongly recommend that this guideline is followed in this study.

(Response) We intend to hold all features other than the manipulations constant in the stimuli.

(Comment 11) From Lilly: One research objective for the main study suggests that the study will measure perceptions of the doctors' acceptance of the drug by respondents. Since respondents will only be seeing a print ad and not interacting with a doctor, we believe the research setting will be too artificial to gain meaningful insights into this topic. We recommend removing the section (questions 21 to 26).

(Response) Please see response to Comment 5 from AbbVie.

(Comment 12) From Lilly: The details of the followup study are less clear than the main study. What are the techniques and what are the dependent measures on which the respondent will be asked to decide?

(Response) The followup study assesses the relative weighting of a market claim and efficacy in decisionmaking. Participants are asked to choose a drug out of two options that vary in (1) the presence of a market claim and (2) efficacy. We will examine product preference as a function of efficacy using logistic regression. The difference in efficacy between the two drugs on each choice set will be a continuous predictor variable and drug choice will be a binary outcome variable. Critically, we will examine whether, and to what extent, the efficacy-choice relationship varies as a function of an added market claim; thus, market claim presence will be an interaction term. The experiment uses a discrete choice approach common in psychology and economics (Ref. 8).

(Comment 13) From Lilly: We suggest FDA stratify the sample for both studies across demographic variables to ensure it is representative of the U.S. diabetic population.

(Response) We are applying demographic quotas to achieve a representative sample.

(Comment 14) From Lilly: The questionnaire employs a number of different Likert scales that differ on the number of scale values and definition of values. Lilly suggests using a standard five-point scale with a mid-point and definitions for each value for all scalar questions.

(Response) We have changed the Likert scales to be internally consistent.

(Comment 15) From Lilly: For questions 9 and 16, by asking the respondents to perceive overall quality of the drug, the survey risks introducing perceptions outside of experimental control into the study. Overall quality is a very broad topic and might be dependent on the graphics, wording, and personal biases that are outside of the market claims and efficacy levels being tested. We suggest removing these questions, or changing the question to "overall efficacy."

(Response) By asking these questions, we hope to detect any differences in perceived quality between those exposed to different experimental conditions. For example, those exposed to an ad with a #1 Prescribed market claim may perceive the product to be of higher quality than those in the control condition. By keeping all ad elements beyond the experimental manipulations (market claims, efficacy claims) constant, we can ensure that significant differences between conditions are a result of the manipulations rather than any extraneous factors. Random assignment to conditions should also distribute any random variance equally across all cells.

(Comment 16) From Lilly: We recommend removing questions 13 and 17 as they have the potential to be misinterpreted or simply difficult for the respondent to answer if the stimulus is not communicating prevalence of the drug's side effects or benefits using precise numbers.

(Response) Please see response to Comment 3 from AbbVie.

(Comment 17) From Lilly: For questions 27 and 28, we recommend slightly changing the wordings for the possible answer choices to "Yes/No, claim is/is not mentioned as a benefit in the ad" for question 27, and "Yes/No, claim is/is not mentioned as a side effect or risk in the ad" for question 28.

(Response) We agree that more specific wording would be helpful and have revised the answer choices to read "Yes, statement is mentioned in the ad" and "No, statement is not mentioned in the ad."

(Comment 18) From Lilly: Recommend removing question 31 as the question is an inverse of question 30 to avoid confounding data.

(Response) We have removed question 31 (skepticism).

(Comment 19) From Lilly: The instructions for the questions 35 through 38 section seem to have an omitted word. We recommend revising to "how much do you agree or disagree with the following statements?"

(Response) Thank you for pointing this out. We will correct this.

(Comment 20) From Lilly: We agree with placement of demographic questions (questions 39-44) at the end but recommend reevaluating them and consider removing them so as to avoid lack of response due to respondent fatigue.

(Response) The comment about respondent fatigue is well taken. However, we are adhering to good questionnaire design in putting our most important dependent measures first and are willing to accept the potential tradeoff in missing demographic data.

(Comment 21) From Lilly: We suggest providing a more complete list of choices for question 43 and placing this question earlier in the study.

(Response) We appreciate this suggestion and have added questions about cost.

(Comment 22) From Merck: Merck supports the importance of communicating information that can be understood by consumers so that they can make better decisions about prescription drugs. We believe that FDA should focus their efforts and research first on improving the health literacy of approved patient labeling and then on DTC print advertising. In addition, FDA should consider exploring the inclusion of benefit information in patient labeling, which may help improve consumer understanding and comprehension of patient labeling.

(Response) We share the goal of improving communications about prescription drugs. There are efforts underway within FDA examining ways to improve patient labeling (Ref. 9). Although this comment is outside the scope of this project, we will share this information internally.

(Comment 23) From Merck: Merck believes the current study design limits the practical utility of the information collected. The study proposes presenting efficacy information in the form of simple quantitative information. Prior OPDP research acknowledged the limitations of studying simple quantitative information. For many prescription drugs, clinical trial outcomes are often more complicated than simple frequencies, which limit the applicability of this research. Numeracy challenges are common in people with inadequate health literacy.

Numeracy challenges are not well represented in online research, and hence the proposed methodology may not detect a lack of comprehension.

(Response) We are pleased Merck has read FDA's prior research in the area of communicating quantitative information. As this is the first study examining the impact of quantitative efficacy information on the perception of market share claims, we felt it was better to start with relatively straightforward, though not simplistic, quantitative efficacy information. We have worked with an expert reviewer in OPDP to product efficacy claims that are realistic for this drug product class. The efficacy claim communicates both the level of expected benefit and the likelihood of experiencing that benefit. We encourage additional research on this topic utilizing increasingly complex quantitative information.

We have included a measure of numeracy in our questionnaire. We acknowledge that online panels may underrepresent individuals with extremely low health literacy. Thus, any differences we find as a function of numeracy in our sample may be magnified in the general population.

(Comment 24) From Merck: Merck recommends a mixed-method approach to reach limited-literacy respondents. The phone or Web approach allows for a broad, diverse geographic sample. Respondents with low health literacy are not typically represented in these databases, and may need to be recruited in less traditional places, such as literacy centers, senior centers, and health clinics. Additionally, if a desktop computer is required, this may inadvertently eliminate respondents from low socioeconomic status, who are less likely to have a desktop computer and more likely to have internet only on their mobile device.

(Response) We acknowledge that internet administration is not perfect and have chosen this method to maximize our budget. We will permit the survey to be taken on a variety of

devices. We are excluding phones because the stimuli cannot be fully viewed on a very small screen.

(Comment 25) From Merck: For the followup study, we recommend reducing the number of trials for respondents across health literacy levels, as respondent fatigue can occur, resulting in reduced focus and unreliably responses. Refining the methodology to present fewer choices to each respondent, and assuring the clarity of the information presented, would help to enhance comprehension.

(Response) We agree that minimizing respondent burden is a priority. We estimate that the 48 trials and instructions would require less than 8 minutes, on average. Pretest data may reveal that the experiment can be shortened without loss to validity, in which case we will reduce the number of trials.

(Comment 26) From Merck: Questions 6, 32, and 50 include percentages. According to Health Literacy Missouri, natural frequencies (1 out of 10) may be more useful than percentages. Research suggests that less literate readers may interpret numbers as more risky when in frequency form (1 out of 10) versus percentage form (10 percent).

(Response) We have worked with an expert reviewer in OPDP to product efficacy claims that are realistic for this drug product class.

(Comment 27) From Merck: We suggest adding the following screener question to increase the odds of recruiting limited-literacy respondents: "How confident are you in filling out medical forms by yourself?"

(Response) We acknowledge that internet panels underrepresent individuals with very low literacy. Thus, it is important to acknowledge that our findings may not apply to very low

literacy individuals. It would be prohibitively expensive for us to screen for literacy up front in order to establish quotas. We will measure health literacy and included it in analyses.

The first two pretests and main study are expected to last no more than 30 minutes. The third pretest and followup study are expected to last no more than 15 minutes. This will be a one-time (rather than annual) collection of information. FDA estimates the burden of this collection of information as follows:

Table 2.--Estimated Burden<sup>1</sup>

Activity	No. of Respondents	No. of Responses per Respondent	Total Respondents	Average Burden per Response	Total Hours
Sample Outgo (Pretests and Main Survey)	16,384	==	==	==	==
Screener Completes	1,638	1	1,638	0.03 (2 minutes)	49.1
Eligible	1,556	==	==	==	==
Completes, Pretest 1	252	1	252	0.5 (30 minutes)	126
Completes, Pretest 2	252	1	252	0.5 (30 minutes)	126
Completes, Main Study	495	1	495	0.5 (30 minutes)	247.5
Completes, Pretest 3	108	1	108	0.25 (15 minutes)	27
Completes, Followup Study	216	1	216	0.25 (15 minutes)	54
Total	==	==	==	==	629.6

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

### III. References

The following references are on display in the Division of Dockets Management (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at <http://www.regulations.gov>. FDA has verified the Web site addresses, as of the date this document publishes in the Federal Register, but Web sites are subject to change over time.

1. Lee, M. and Y-C. Lou, "Consumer Reliance on Intrinsic and Extrinsic Cues in Product Evaluations: A Conjoint Approach," Journal of Applied Business Research, 12(1):21-29, 2011.
2. Teas, R.K. and S. Agarwal, "The Effects of Extrinsic Product Cues on Consumers' Perceptions of Quality, Sacrifice, and Value," Journal of the Academy of Marketing Science, 28(2):278-290, 2000.
3. Rao, A.R. and K. B. Monroe, "The Effect of Price, Brand Name, and Store Name on Buyers' Perceptions of Product Quality: An Integrative Review," Journal of Marketing Research, 26(3):351-357, 1989.
4. Mitra, A., J.L. Swasy, and K.J. Aikin, "How Do Consumers Interpret Market Leadership Claims in Direct-to-Consumer Advertising of Prescription Drugs?" Advances in Consumer Research, 33:381-387, 2006.
5. O'Donoghue, A.C., H.W. Sullivan, K.J. Aikin, et al., "Presenting Efficacy Information in Direct-to-Consumer Prescription Drug Advertisements," Patient Education and Counseling, 95(2):271-280, 2014.
6. Schwartz, L.M., S. Woloshin, and H.G. Welch, "Using a Drug Facts Box to Communicate Drug Benefits and Harms: Two Randomized Trials," Annals of Internal Medicine, 150(8):516-527, 2009.
7. Sullivan, H. W., A.C. O'Donoghue, and K.J. Aikin, "Presenting Quantitative Information About Placebo Rates to Patients," JAMA Internal Medicine, 173(2):2006-2007, 2013.
8. Train, K. E., Discrete Choice Methods With Simulation, Cambridge University Press, 2009.



9. Boudewyns, V., A. C. O'Donoghue, B. Kelly, et al, "Influence of Patient Medication Information Format on Comprehension and Application of Medication Information: A Randomized, Controlled Experiment," Patient Education and Counseling, 98(12):1592-1599, 2015.

Dated: April 28, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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